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Dr. Edward A. Steinhaus
Department of Biological Control
Laboratory of Insect Pathology
University of California
Berkeley 4, California

Dear Ed:

How can one give a definite answer to your question, knowing as little as we do about the genetics of virulence?

My own opinion concurs with yours, that it would be as likely that other commonly used microbes should become pathogenic for man. I suppose there is some risk attached to the introduction of any new agent, biological or chemical, into our environment. For example, it is plausible that one human in, say, ten thousand might be exquisitely sensitive, owing to his particular genetic constitution, to some new chemical insecticide. Not many preliminary safety tests could pick that up!

Suppose Bacillus thuringiensis did mutate into B. anthracis (preposterous as this may seem). Would the very rare incidence of such an event add significantly to human risks? It would only if we already lived in an environment that was totally free of anthrax, which is not the case.

My general attitude is that one should be cautious about releasing any new agent. If your large scale empirical tests show no overt risk, I don't think the possibility of rare mutation adds very much, when the conditions of use are such that rare mutants would be added to an already existing reservoir of possible infection. I would worry about mutation from B. thuringiensis -- B. anthrax as little, and as much, as I would cereus -- anthrax.

Any biological product ought to be administered with some care. If the Bacillus spores are good antigens, as they may well be, they stand a good chance of provoking allergic reactions in a minority of handlers, especially if handled carelessly.

In the long run, we will have to use empirical criteria to judge the absolute safety of insect pathogens for control. One wishes that the producers of chemical insecticides were as sensitive to remote

possibilities of human risks from their products as may apply to these microorganisms. It is possible to raise as many hypothetical possibilities of trouble for one as for the other; if we are to have any chance of progress at all, we have to take a balanced view, and accept some remote risks, after a strenuous regime of empirical safety testing.

Yours sincerely,

Joshua Lederberg
Professor of Medical Genetics

JL/ew

P. S. Have you any recent word on the Buchner translation project?